

What is claimed is:

1. A method of inhibiting activation of a human α_{1d} adrenergic receptor which comprises contacting the receptor with a compound so as to inhibit activation of the receptor, wherein the compound binds to the human α_{1d} adrenergic receptor with a binding affinity which is at least ten-fold higher than the binding affinity with which the compound binds to (i) a human α_{1a} adrenergic receptor and (ii) a human α_{1b} adrenergic receptor, and the compound binds to the human α_{1d} adrenergic receptor with a binding affinity which is greater than the binding affinity with which the compound binds to a human 5-HT_{1a} receptor.
2. The method of claim 1, wherein the compound binds to the human α_{1d} adrenergic receptor with a binding affinity which is at least 25-fold higher than the binding affinity with which the compound binds to (i) the human α_{1a} adrenergic receptor and (ii) the human α_{1b} adrenergic receptor, and the compound binds to the human α_{1d} adrenergic receptor with a binding affinity which is at least ten-fold higher than the binding affinity with which the compound binds to the human 5-HT_{1a} receptor.
3. The method of claim 2, wherein the compound binds to the human α_{1d} adrenergic receptor with a binding affinity which is at least 25-fold higher than the binding affinity with which the compound binds to (i) the human α_{1a} adrenergic receptor, (ii) the human α_{1b} adrenergic receptor, and (iii) the human 5-HT_{1a} receptor.
4. The method of claim 3, wherein the compound binds to

Sub B1

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ger fr



ger fr



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unbranched C₁-C₆ hydroxyalkyl, hydroxy, substituted
or unsubstituted aryl or aryl-(C₁-C₆)-alkyl, or
substituted or unsubstituted heteroaryl or
heteroaryl-(C₁-C₆)-alkyl, wherein the substituent if
present is a halogen, CN, nitro, hydroxy, branched
or unbranched C₁-C₆ alkyl or alkoxy group, or
branched or unbranched C₂-C₆ alkenyl or alkynyl
group; or (ii) taken together form a substituted or
unsubstituted cycloalkyl ring containing 3-10
carbons, wherein the substituent if present is a
branched or unbranched C₁-C₆ alkyl group or branched
or unbranched C₂-C₆ alkenyl or alkynyl group;

wherein R₃ is H, branched or unbranched C₁-C₆ alkyl,
branched or unbranched C₂-C₆ alkenyl or alkynyl, C₃-C₇
cycloalkyl, C₃-C₇ cycloalkylalkyl, aryl, heteroaryl,
aryl-(C₁-C₆)-alkyl, heteroaryl-(C₁-C₆)-alkyl,
substituted C₁-C₆ alkyl, substituted C₃-C₇ cycloalkyl,
substituted aryl, substituted heteroaryl,
substituted aryl-(C₁-C₆)-alkyl, or substituted
heteroaryl-(C₁-C₆)-alkyl, wherein the substituent if
present is a halogen, CN, nitro, C₁-C₆ alkyl, OR₁₄,
SR₁₄, N(R₁₄)₂, SO₂N(R₁₄)₂, CO₂R₁₄, SO₃R₁₄,
N(R₁₄)COR₁₄, CON(R₁₄)₂, or N(R₁₄)CON(R₁₄)₂;

wherein R₄ is H or CH₃;

wherein R₅ is H, branched or unbranched C₁-C₆ alkyl,
branched or unbranched C₂-C₆ alkenyl or alkynyl, C₃-C₇
cycloalkyl, C₃-C₇ cycloalkylalkyl, aryl, heteroaryl,
aryl-(C₁-C₆)-alkyl, heteroaryl-(C₁-C₆)-alkyl,
substituted C₁-C₆ alkyl, substituted C₃-C₇ cycloalkyl,
substituted aryl, substituted heteroaryl,
substituted aryl-(C₁-C₆)-alkyl, or substituted
heteroaryl-(C₁-C₆)-alkyl, wherein the substituent if

present is a halogen, CN, nitro, C₁-C₆ alkyl, OR₁₄, SR₁₄, N(R₁₄)₂, SO₂N(R₁₄)₂, CO₂R₁₄, SO₃R₁₄, N(R₁₄)COR₁₄, CON(R₁₄)₂, or N(R₁₄)CON(R₁₄)₂;

5 wherein R₆ is H, branched or unbranched C₁-C₆ alkyl, branched or unbranched C₂-C₆ alkenyl or alkynyl, C₃-C₇ cycloalkyl, C₃-C₇ cycloalkylalkyl, aryl, heteroaryl, aryl-(C₁-C₆)-alkyl, heteroaryl-(C₁-C₆)-alkyl, substituted C₁-C₆ alkyl, substituted C₃-C₇ cycloalkyl, substituted aryl, substituted heteroaryl, substituted aryl-(C₁-C₆)-alkyl, or substituted
10 heteroaryl-(C₁-C₆)-alkyl, wherein the substituent if present is a halogen, CN, nitro, C₁-C₆ alkyl, OR₁₄, SR₁₄, N(R₁₄)₂, SO₂N(R₁₄)₂, CO₂R₁₄, SO₃R₁₄, N(R₁₄)COR₁₄, CON(R₁₄)₂, or N(R₁₄)CON(R₁₄)₂;

15 wherein R₇ is H, branched or unbranched C₁-C₆ alkyl, branched or unbranched C₂-C₆ alkenyl or alkynyl, C₃-C₇ cycloalkyl, aryl, aryl-(C₁-C₆)-alkyl, CO₂R₁₄, CON(R₁₄)₂, substituted C₁-C₆ alkyl, substituted aryl, wherein the substituent is N(R₁₄)₂, halogen, OR₁₄ or
20 SR₁₄;

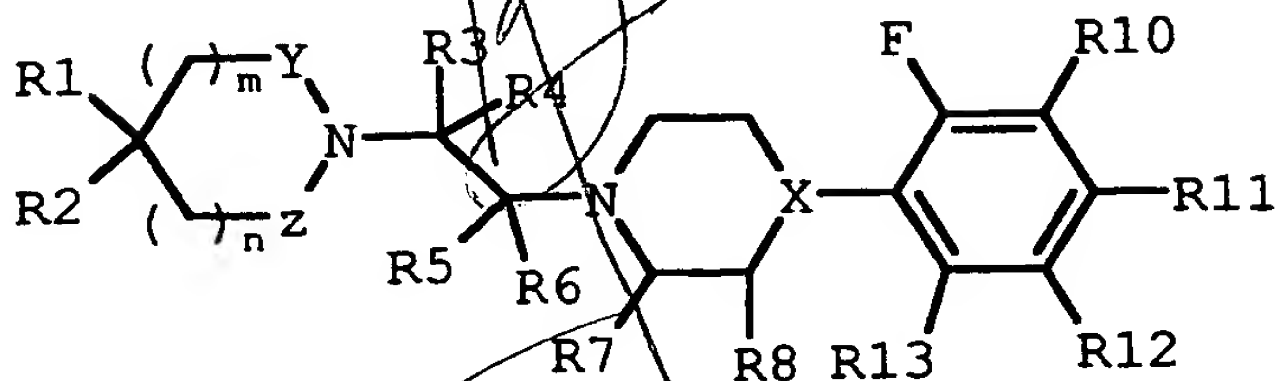
wherein R₈ is H or CH₃;

wherein R₉ is H, F, Cl, Br, branched or unbranched C₁-C₆ alkyl or alkoxy, CN; wherein R₁₀ is H or F; wherein R₁₁ is H, F, Cl, Br, I, CN, branched or
25 unbranched C₁-C₆ alkyl or alkoxy; wherein R₁₂ is H, F, Cl, CN, branched or unbranched C₁-C₆ alkyl or alkoxy; wherein R₁₃ is H or F; wherein X is N or CH; with the proviso that when R₁₁ and R₁₂ are each H, then R₉ is F;

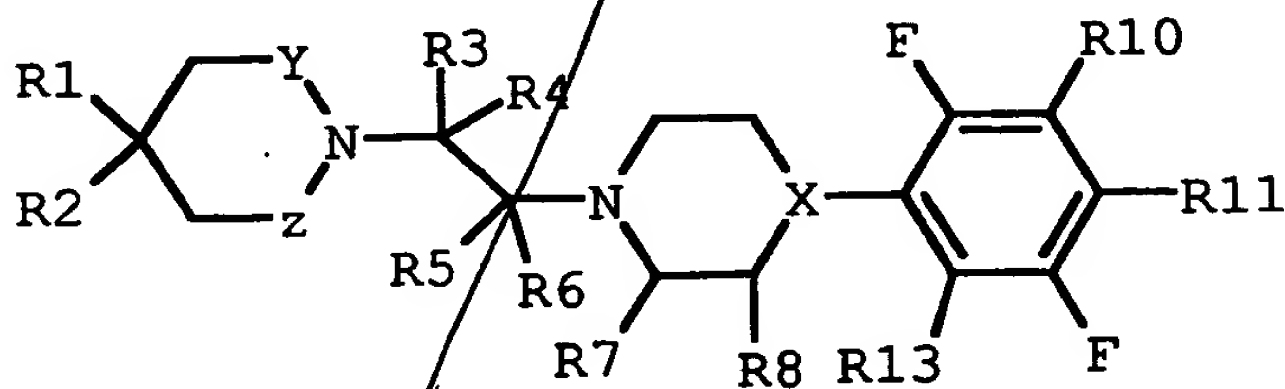
30 and wherein R₁₄ is independently H or branched or

unbranched C₁-C₆ alkyl.

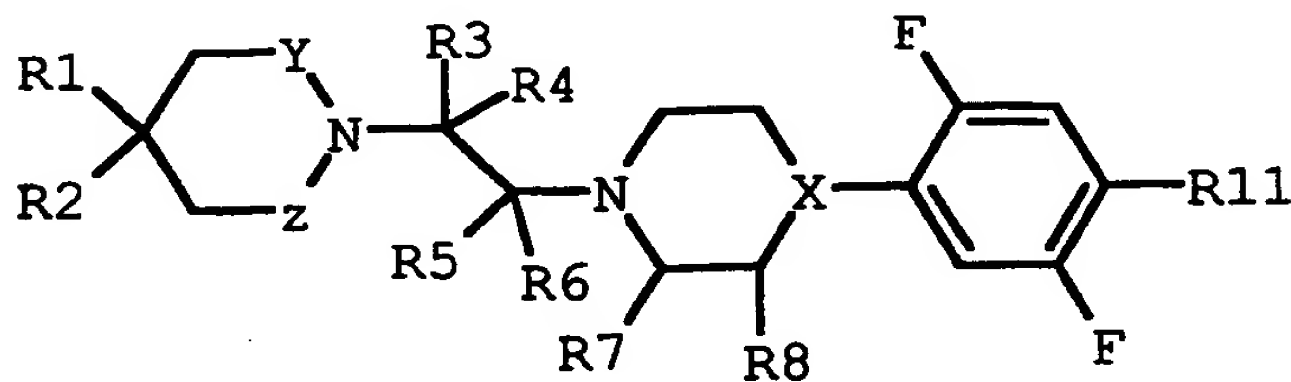
6. The method of claim 5, wherein the compound has the structure:



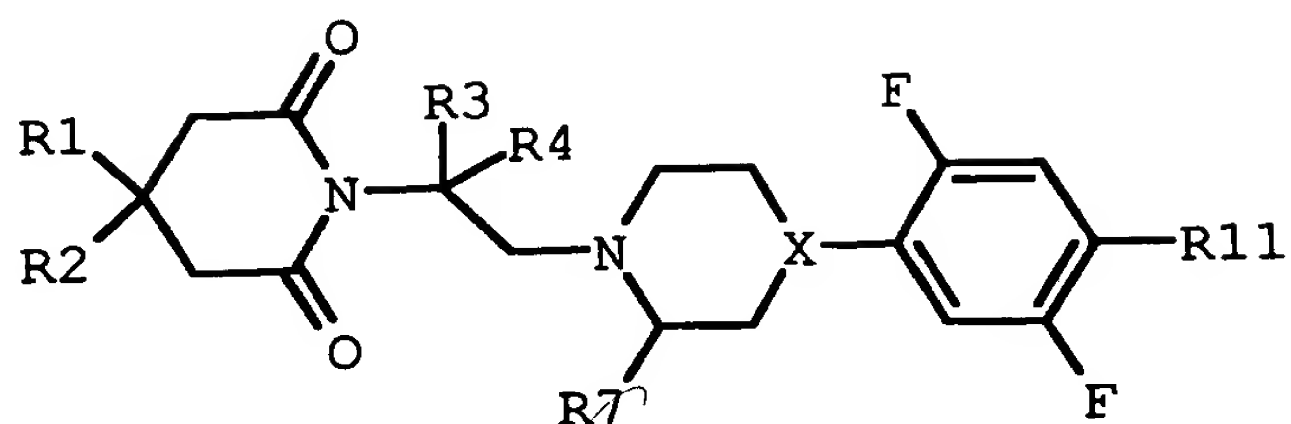
7. The method of claim 6, wherein the compound has the structure:



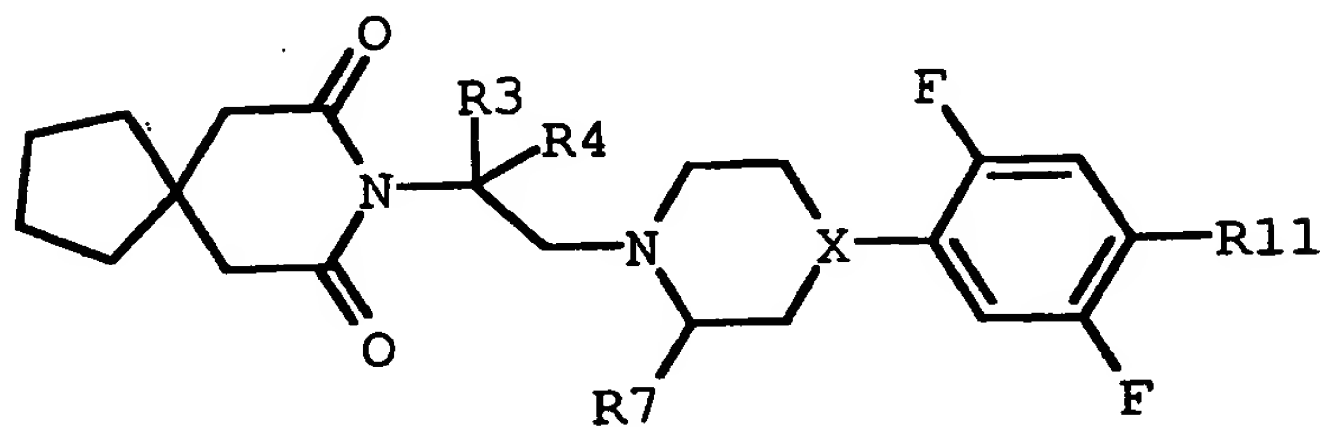
8. The method of claim 7, wherein the compound has the structure:



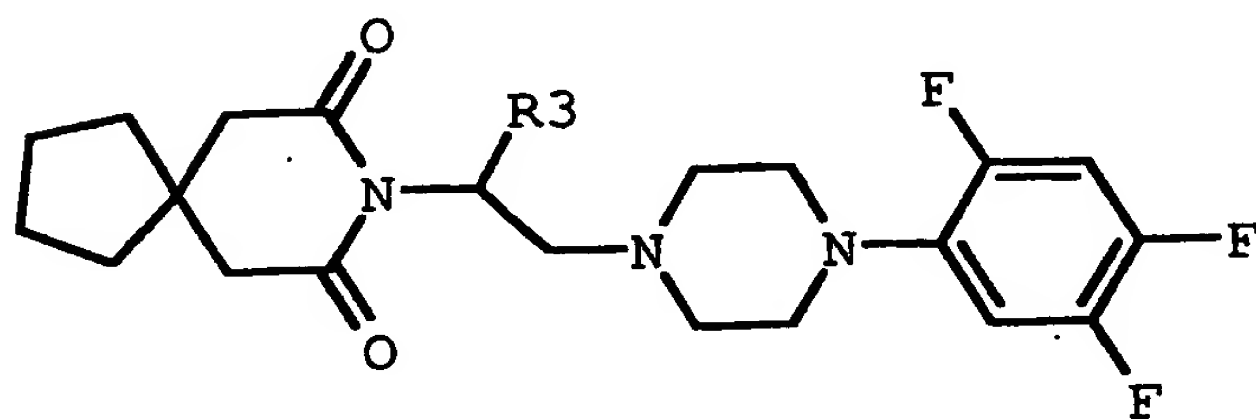
9. The method of claim 8, wherein the compound has the structure:



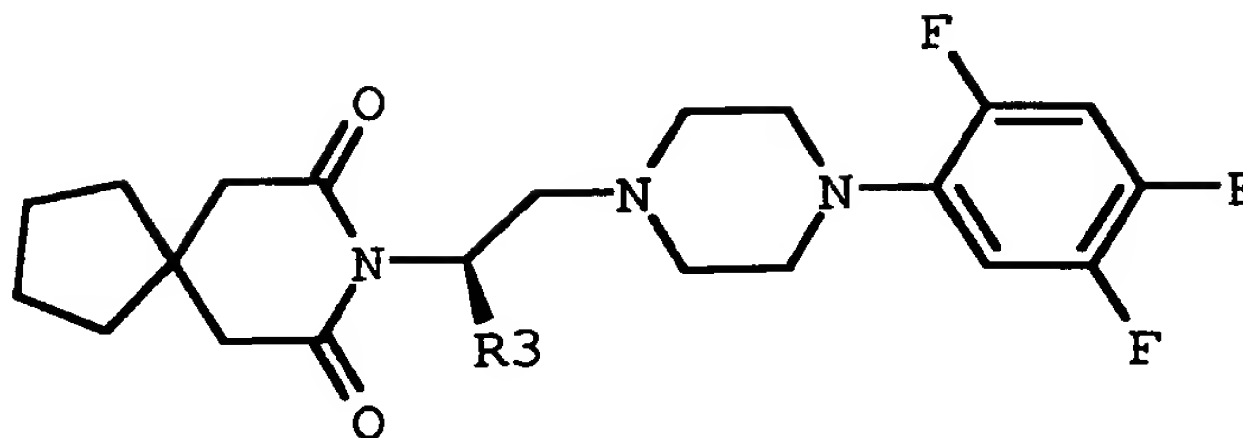
10. The method of claim 9, wherein the compound has the structure:



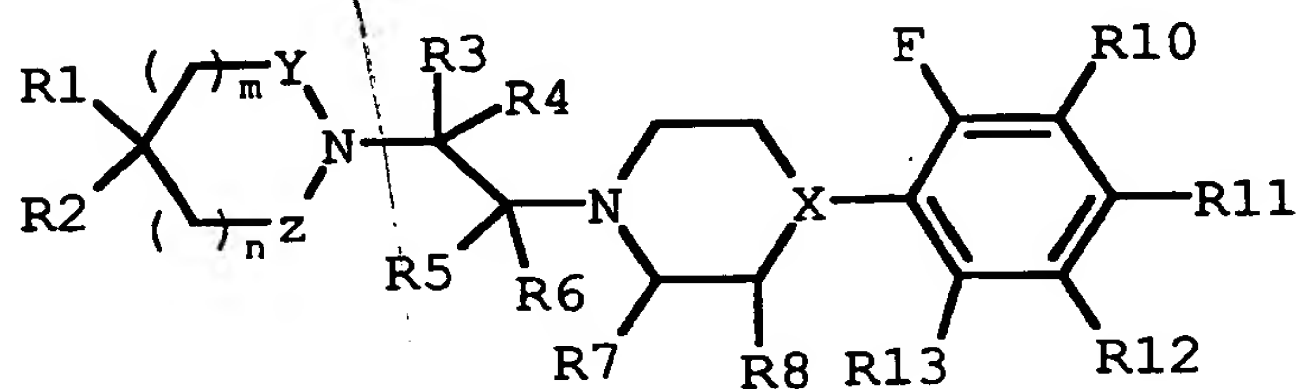
- 5 11. The method of claim 10, wherein the compound has the structure:



12. The method of claim 11, wherein the compound has the structure:

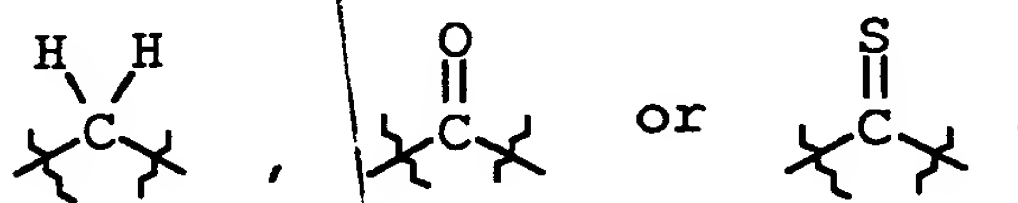


13. A compound having the structure:

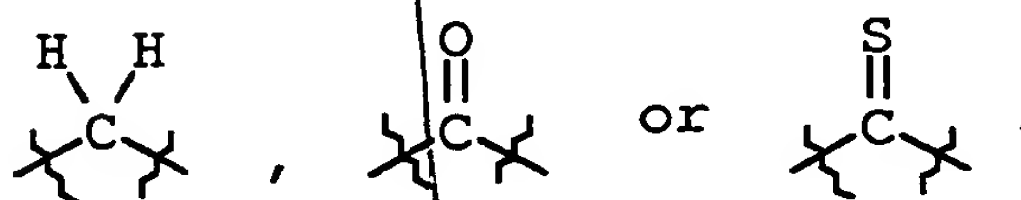


wherein n is an integer from 0 to 2; wherein m is an integer from 0 to 2;

wherein Y is



wherein Z is



wherein R1 and R2 (i) are independently H, branched or unbranched C₁-C₆ alkyl or alkoxy, branched or unbranched C₂-C₆ alkenyl or alkynyl, branched or unbranched C₁-C₆ hydroxyalkyl, hydroxy, substituted or unsubstituted aryl or aryl-(C₁-C₆)-alkyl, or substituted or unsubstituted heteroaryl or heteroaryl-(C₁-C₆)-alkyl, wherein the substituent if present is a halogen, CN, nitro, hydroxy, branched or unbranched C₁-C₆ alkyl or alkoxy group, or branched or unbranched C₂-C₆ alkenyl or alkynyl group; or (ii) taken together form a substituted or unsubstituted cycloalkyl ring containing 3-10 carbons, wherein the substituent if present is a branched or unbranched C₁-C₆ alkyl group or branched or unbranched C₂-C₆ alkenyl or alkynyl group;

wherein R3 is H, branched or unbranched C₁-C₆ alkyl, branched or unbranched C₂-C₆ alkenyl or alkynyl, C₃-C₇ cycloalkyl, C₃-C₇ cycloalkylalkyl, aryl, heteroaryl, aryl-(C₁-C₆)-alkyl, heteroaryl-(C₁-C₆)-alkyl, substituted C₁-C₆ alkyl, substituted C₃-C₇ cycloalkyl, substituted aryl, substituted heteroaryl, substituted aryl-(C₁-C₆)-alkyl, or substituted heteroaryl-(C₁-C₆)-alkyl, wherein the substituent if present is a halogen, CN, nitro, C₁-C₆ alkyl, OR₁₄, SR₁₄, N(R₁₄)₂, SO₂N(R₁₄)₂, CO₂R₁₄, SO₃R₁₄, N(R₁₄)COR₁₄, CON(R₁₄)₂, or N(R₁₄)CON(R₁₄)₂;

wherein R4 is H or CH₃;

wherein R5 is H, branched or unbranched C₁-C₆ alkyl, branched or unbranched C₂-C₆ alkenyl or alkynyl, C₃-C₇ cycloalkyl, C₃-C₇ cycloalkylalkyl, aryl, heteroaryl, aryl-(C₁-C₆)-alkyl, heteroaryl-(C₁-C₆)-alkyl, substituted C₁-C₆ alkyl, substituted C₃-C₇ cycloalkyl,

substituted aryl, substituted heteroaryl,
substituted aryl-(C₁-C₆)-alkyl, or substituted
heteroaryl-(C₁-C₆)-alkyl, wherein the substituent if
present is a halogen, CN, nitro, C₁-C₆ alkyl, OR₁₄,
SR₁₄, N(R₁₄)₂, SO₂N(R₁₄)₂, CO₂R₁₄, SO₃R₁₄,
N(R₁₄)COR₁₄, CON(R₁₄)₂, or N(R₁₄)CON(R₁₄)₂;

wherein R₆ is H, branched or unbranched C₁-C₆ alkyl,
branched or unbranched C₂-C₆ alkenyl or alkynyl, C₃-C₇
cycloalkyl, C₃-C₇ cycloalkylalkyl, aryl, heteroaryl,
aryl-(C₁-C₆)-alkyl, heteroaryl-(C₁-C₆)-alkyl,
substituted C₁-C₆ alkyl, substituted C₃-C₇ cycloalkyl,
substituted aryl, substituted heteroaryl,
substituted aryl-(C₁-C₆)-alkyl, or substituted
heteroaryl-(C₁-C₆)-alkyl, wherein the substituent if
present is a halogen, CN, nitro, C₁-C₆ alkyl, OR₁₄,
SR₁₄, N(R₁₄)₂, SO₂N(R₁₄)₂, CO₂R₁₄, SO₃R₁₄,
N(R₁₄)COR₁₄, CON(R₁₄)₂, or N(R₁₄)CON(R₁₄)₂;

wherein R₇ is H, branched or unbranched C₁-C₆ alkyl,
branched or unbranched C₂-C₆ alkenyl or alkynyl, C₃-C₇
cycloalkyl, aryl, aryl-(C₁-C₆)-alkyl, CO₂R₁₄,
CON(R₁₄)₂, substituted C₁-C₆ alkyl, substituted aryl,
wherein the substituent is N(R₁₄)₂, halogen, OR₁₄ or
SR₁₄;

wherein R₈ is H or CH₃;

wherein R₁₀ is H or F; wherein R₁₁ is H, F, Cl, Br,
I, CN, branched or unbranched C₁-C₆ alkyl or alkoxy;
wherein R₁₂ is H, F, Cl, CN, branched or unbranched
C₁-C₆ alkyl or alkoxy; wherein R₁₃ is H or F; wherein
X is N or CH; and wherein R₁₄ is independently H or
branched or unbranched C₁-C₆ alkyl.

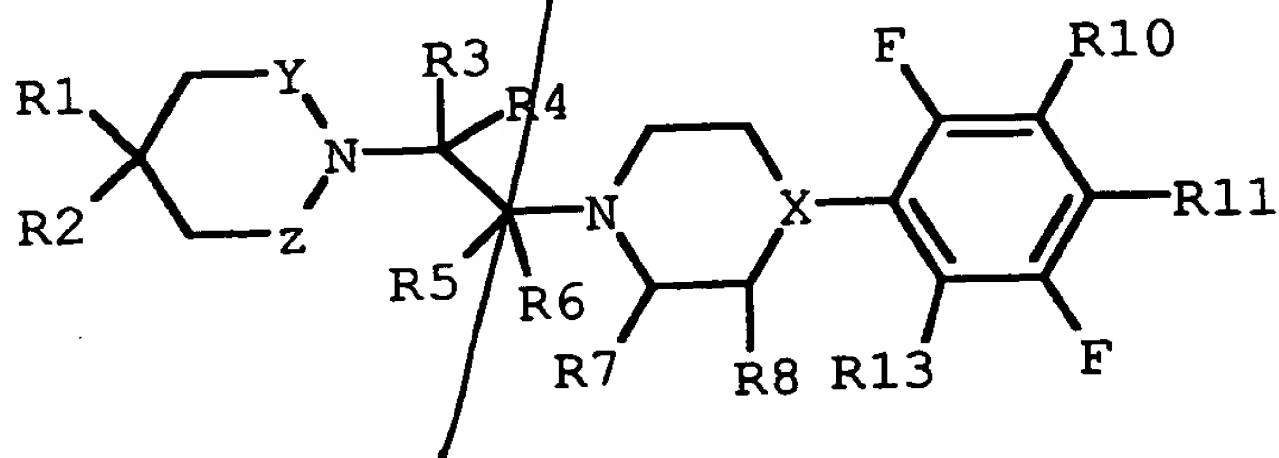
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14. A compound of claim 13, wherein the compound comprises the (+) enantiomer.

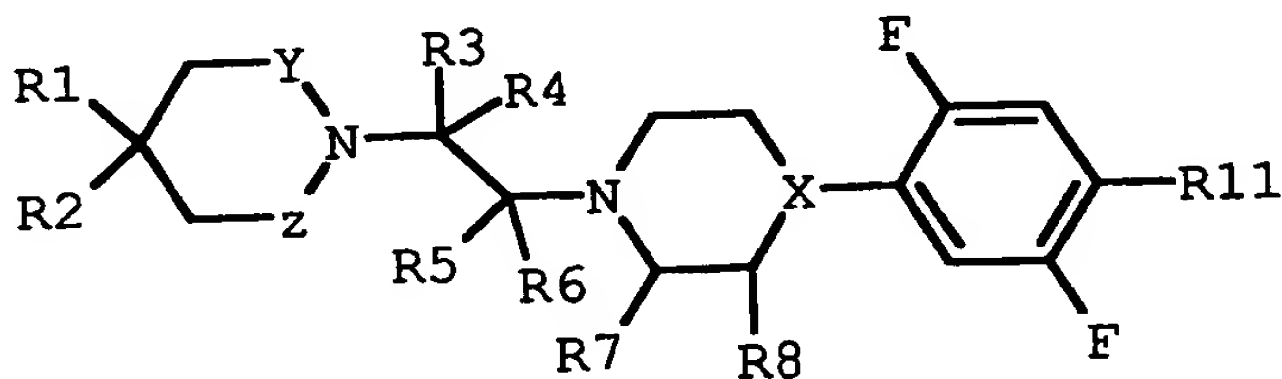
15. A compound of claim 13, wherein the compound comprises the (-) enantiomer.

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16. A compound of claim 13, wherein the compound has the structure:

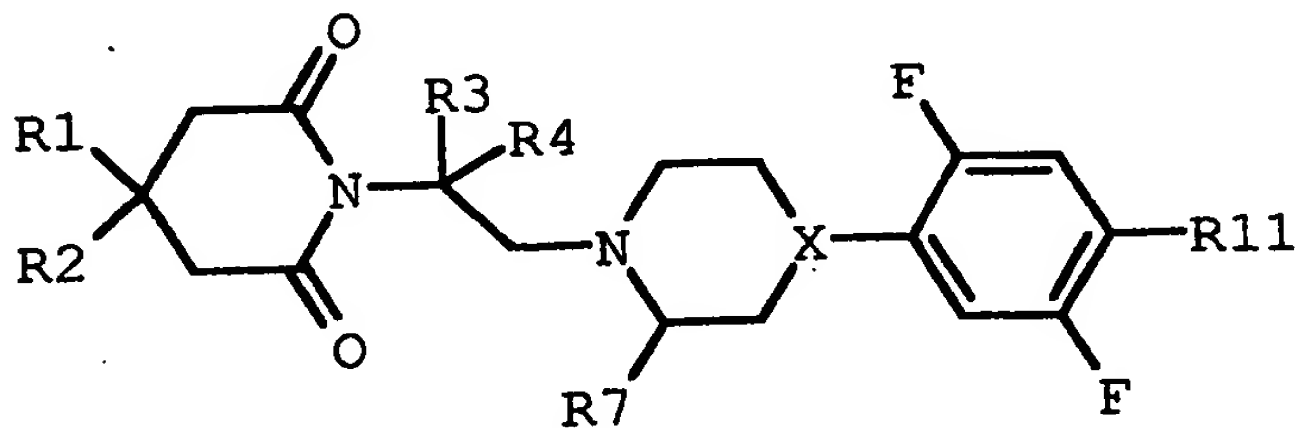


17. A compound of claim 16, wherein the compound has the structure:

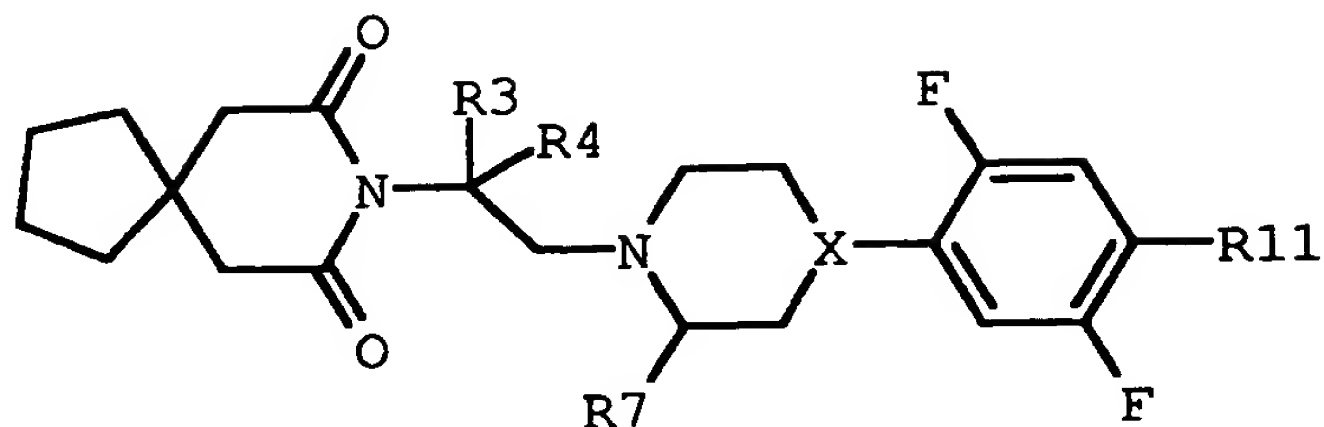


18. A compound of claim 17, wherein the compound has the structure:

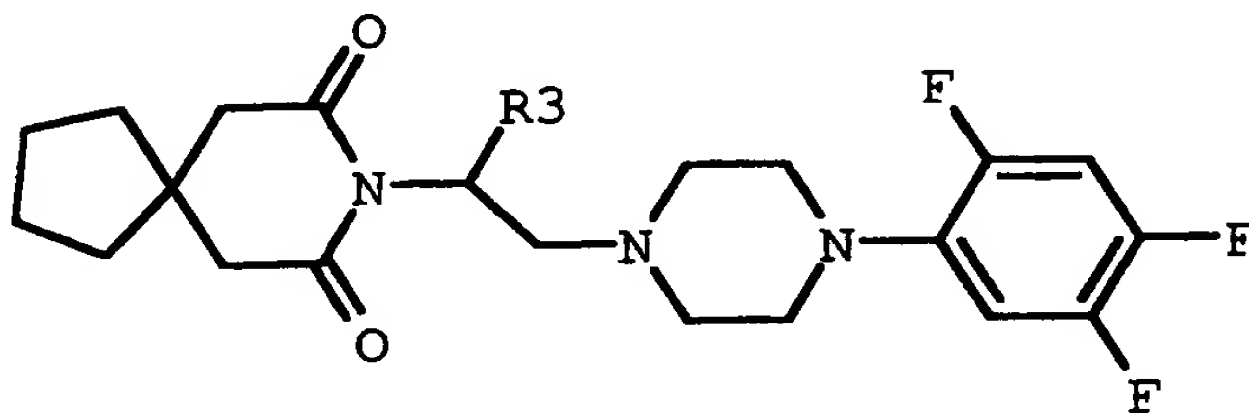
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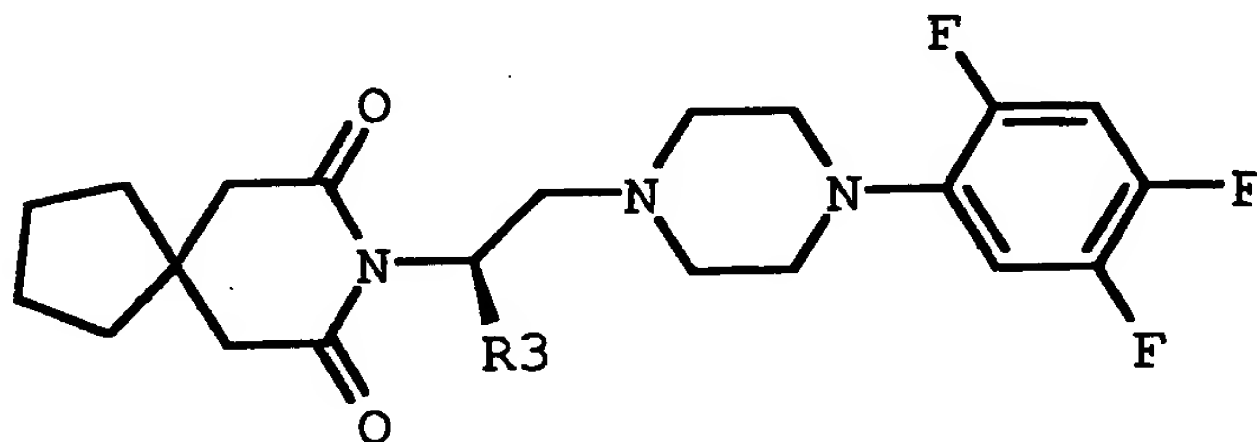
19. A compound of claim 18, wherein the compound has the structure:



20. A compound of claim 19, wherein the compound has the structure:



21. A compound of claim 20, wherein the compound has the structure:



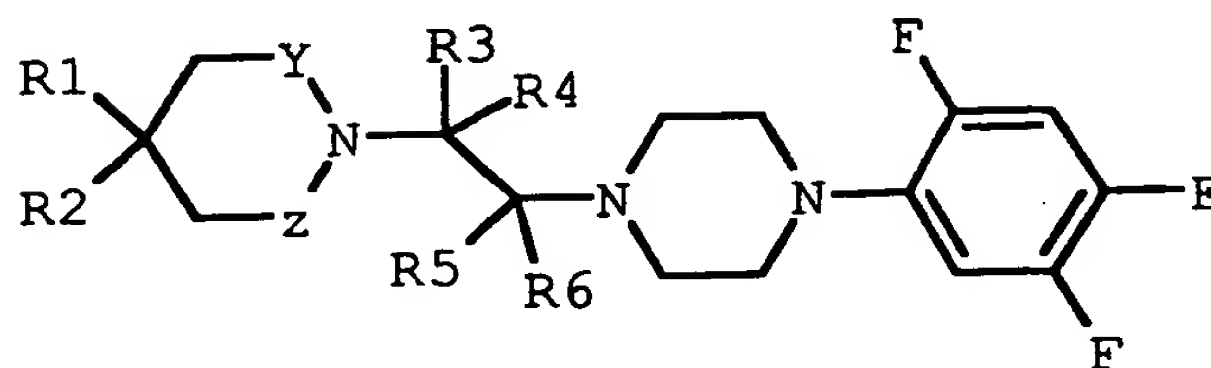
22. A pharmaceutical composition comprising a therapeutically effective amount of the compound of claim 13 and a pharmaceutically acceptable carrier.

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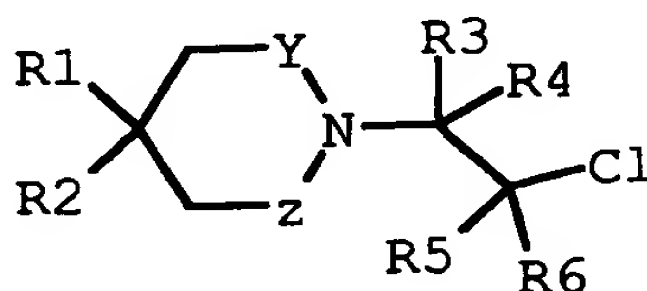
23. The pharmaceutical composition of claim 22, wherein the amount of the compound is an amount from about 0.01 mg to about 800 mg.
- 5 24. The pharmaceutical composition of claim 23, wherein the amount of the compound is from about 0.1 mg to about 300 mg.
25. The pharmaceutical composition of claim 24, wherein the amount of the compound is from about 1 mg to about 20 mg.
- 10 26. The pharmaceutical composition of claim 22, wherein the carrier is a liquid.
27. The pharmaceutical composition of claim 22, wherein the carrier is a solid.
- 15 28. The pharmaceutical composition of claim 22, wherein the carrier is a gel.
29. A pharmaceutical composition obtained by combining a therapeutically effective amount of a compound of claim 13 and a pharmaceutically acceptable carrier.
- 20 30. A process for making a pharmaceutical composition comprising combining a therapeutically effective amount of a compound of claim 13 and a pharmaceutically acceptable carrier.

*Ans
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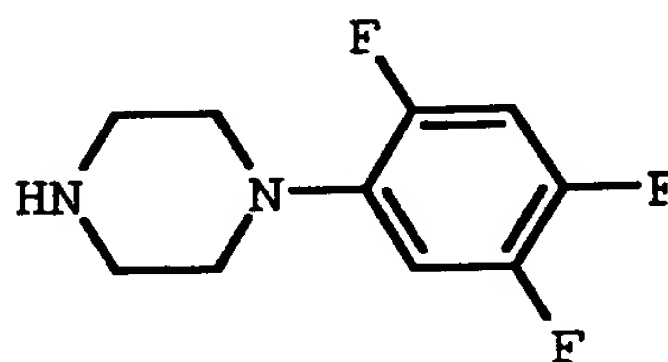
31. A process of making a compound with structure:



which comprises reacting a compound with structure:



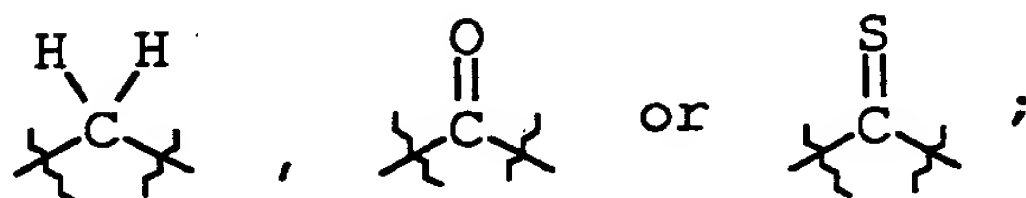
with a compound



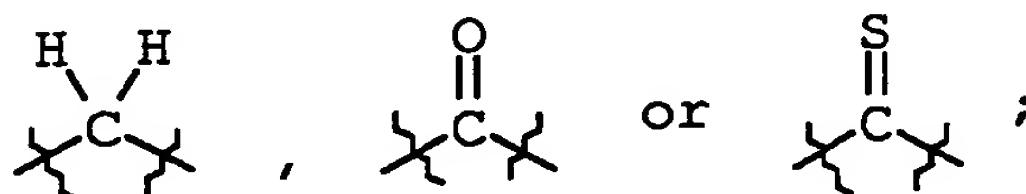
to form the compound,

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wherein Y is



wherein Z is



wherein R1 and R2 (i) are independently H, branched or unbranched C₁-C₆ alkyl or alkoxy, branched or unbranched C₂-C₆ alkenyl or alkynyl, branched or unbranched C₁-C₆ hydroxyalkyl, hydroxy, substituted or unsubstituted aryl or aryl-(C₁-C₆)-alkyl, or substituted or unsubstituted heteroaryl or heteroaryl-(C₁-C₆)-alkyl, wherein the substituent if present is a halogen, CN, nitro, hydroxy, branched or unbranched C₁-C₆ alkyl or alkoxy group, or branched or unbranched C₂-C₆ alkenyl or alkynyl group; or (ii) taken together form a substituted or unsubstituted cycloalkyl ring containing 3-10 carbons, wherein the substituent if present is a branched or unbranched C₁-C₆ alkyl group or branched or unbranched C₂-C₆ alkenyl or alkynyl group;

wherein R3 is H, branched or unbranched C₁-C₆ alkyl, branched or unbranched C₂-C₆ alkenyl or alkynyl, C₃-C₇ cycloalkyl, C₃-C₇ cycloalkylalkyl, aryl, heteroaryl, aryl-(C₁-C₆)-alkyl, heteroaryl-(C₁-C₆)-alkyl, substituted C₁-C₆ alkyl, substituted C₃-C₇ cycloalkyl, substituted aryl, substituted heteroaryl, substituted aryl-(C₁-C₆)-alkyl, or substituted heteroaryl-(C₁-C₆)-alkyl, wherein the substituent if present is a halogen, CN, nitro, C₁-C₆ alkyl, OR₁₄, SR₁₄, N(R₁₄)₂, SO₂N(R₁₄)₂, CO₂R₁₄, SO₃R₁₄, N(R₁₄)COR₁₄, CON(R₁₄)₂, or N(R₁₄)CON(R₁₄)₂;

wherein R4 is H or CH₃;

wherein R5 is H, branched or unbranched C₁-C₆ alkyl, branched or unbranched C₂-C₆ alkenyl or alkynyl, C₃-C₇ cycloalkyl, C₃-C₇ cycloalkylalkyl, aryl, heteroaryl, aryl-(C₁-C₆)-alkyl, heteroaryl-(C₁-C₆)-alkyl, substituted C₁-C₆ alkyl, substituted C₃-C₇ cycloalkyl, substituted aryl, substituted heteroaryl, substituted aryl-(C₁-C₆)-alkyl, or substituted heteroaryl-(C₁-C₆)-alkyl, wherein the

substituent if present is a halogen, CN, nitro, C₁-C₆ alkyl, OR₁₄, SR₁₄, N(R₁₄)₂, SO₂N(R₁₄)₂, CO₂R₁₄, SO₃R₁₄, N(R₁₄)COR₁₄, CON(R₁₄)₂, or N(R₁₄)CON(R₁₄)₂;

wherein R₆ is H, branched or unbranched C₁-C₆ alkyl, branched or unbranched C₂-C₆ alkenyl or alkynyl, C₃-C₇ cycloalkyl, C₃-C₇ cycloalkylalkyl, aryl, heteroaryl, aryl-(C₁-C₆)-alkyl, heteroaryl-(C₁-C₆)-alkyl, substituted C₁-C₆ alkyl, substituted C₃-C₇ cycloalkyl, substituted aryl, substituted heteroaryl, substituted aryl-(C₁-C₆)-alkyl, or substituted heteroaryl-(C₁-C₆)-alkyl, wherein the substituent if present is a halogen, CN, nitro, C₁-C₆ alkyl, OR₁₄, SR₁₄, N(R₁₄)₂, SO₂N(R₁₄)₂, CO₂R₁₄, SO₃R₁₄, N(R₁₄)COR₁₄, CON(R₁₄)₂, or N(R₁₄)CON(R₁₄)₂; and wherein R₁₄ is independently H or branched or unbranched C₁-C₆ alkyl.

32. A method of treating a subject afflicted with a disease which is susceptible to treatment by antagonism of the human α_{1d} adrenergic receptor which comprises administering to the subject an amount of the compound of claim 13 effective to treat the disease.

33. A method of treating a subject afflicted with hypertension which comprises administering to the subject an amount of the compound of claim 13 effective to treat hypertension.

34. A method of treating a subject afflicted with Raynaud's disease which comprises administering to the subject an amount of the compound of claim 13 effective to treat Raynaud's disease.

35. A method of claim 34, wherein the compound

additionally does not cause hypotension at dosages effective to treat Raynaud's disease.

36. A method of treating a subject afflicted with urinary incontinence which comprises administering to the subject an amount of the compound of claim 13 effective to treat urinary incontinence.

37. A method of claim 36, wherein the compound additionally does not cause hypotension at dosages effective to treat urinary incontinence.

38. A method of treating urinary incontinence in a subject which comprises administering to the subject a therapeutically effective amount of a α_{1d} antagonist which binds to the human α_{1d} adrenergic receptor with a binding affinity which is at least ten-fold higher than the binding affinity with which the α_{1d} antagonist binds to (i) a human α_{1a} adrenergic receptor and (ii) a human α_{1b} adrenergic receptor, and the α_{1d} antagonist binds to the human α_{1d} adrenergic receptor with a binding affinity which is greater than the binding affinity with which the α_{1d} antagonist binds to a human 5-HT_{1a} receptor.

39. The method of claim 38, wherein the α_{1d} antagonist binds to the human α_{1d} adrenergic receptor with a binding affinity which is at least 25-fold higher than the binding affinity with which the α_{1d} antagonist binds to (i) the human α_{1a} adrenergic receptor and (ii) the human α_{1b} adrenergic receptor, and the α_{1d} antagonist binds to the human α_{1d} adrenergic receptor with a binding affinity which is at least ten-fold higher than the binding affinity with which the α_{1d} antagonist binds to the human 5-

HT_{1a} receptor.

- 5 40. The method of claim 39, wherein the α_{1d} antagonist binds to the human α_{1d} adrenergic receptor with a binding affinity which is at least 25-fold higher than the binding affinity with which the α_{1d} antagonist binds to (i) the human α_{1a} adrenergic receptor, (ii) the human α_{1b} adrenergic receptor, and (iii) the human 5-HT_{1a} receptor.
- 10 41. The method of claim 40, wherein the α_{1d} antagonist binds to the human α_{1d} adrenergic receptor with a binding affinity which is at least 100-fold higher than the binding affinity with which the α_{1d} antagonist binds to (i) the human α_{1a} adrenergic receptor, (ii) the human α_{1b} adrenergic receptor, and (iii) the human 5-HT_{1a} receptor.
- 15 42. A method of claim 38, wherein the α_{1d} antagonist additionally does not cause hypotension at dosages effective to treat urinary incontinence.